

00/13/00
Old S. U. S. 2990UTILITY
PATENT APPLICATION
TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No. 000687.00138

First Inventor or Application Identifier José TAMEZ-PENÁ

Title MAGNETIC RESONANCE IMAGING WITH RESOLUTION
CONTRAST ENHANCEMENT

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents

ADDRESS TO: Assistant Commissioner for Patents
Box Patent Application
Washington, DC 20231

1. ☒ Fee Transmittal Form (e.g. PTO/SB/17)
(Submit an original and a duplicate for fee processing)
2. ☒ Specification Total Pages **23**
3. ☒ Drawing(s) (35 U.S.C. 113) Total Sheets **7**
4. ☐ Oath or Declaration Total Pages **2**
- a. ☒ Newly executed (original or copy)
- b. ☐ Copy from a prior application (37 C.F.R. §1.63(d))
(for continuation/divisional with box 15 completed)
- i. ☐ DELETION OF INVENTOR(S)
Signed statement attached deleting inventor(s) named
in the prior application, see 37 C.F.R. §1.63(d)(2) and
1.33(b).
5. ☐ Incorporation By Reference (usable if box 4B is checked)
(The entire disclosure of the prior application, from which a copy of the
oath or declaration is supplied under box 4B, is considered to be part
of the disclosure of the accompanying application and is hereby
incorporated by reference therein.)

ACCOMPANYING APPLICATION PARTS

6. ☒ Assignment Papers (cover sheet & document(s))
7. ☐ 37 C.F.R. §3.73(b) Statement ☐ Power of Attorney
(when there is an assignee)
8. ☐ English Translation Document (if applicable)
9. ☐ Information Disclosure
Statement (IDS)/PTO-1449 ☐ Copies of IDS
Citations
10. ☐ Preliminary Amendment
11. ☒ White Advance Serial No. Postcard
12. ☒ Small Entity
Statement(s) ☐ Statement filed in prior
application. Status still proper
and desired.
13. ☐ Certified Copy of Priority Document(s)
(if foreign priority is claimed)
14. ☐ Other:

15. If a CONTINUING APPLICATION, check appropriate box, and supply the requisite information below:

- ☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application no.:
Prior application information: Examiner: Group Art Unit:

16. Amend the specification by inserting before the first line the sentence:

- ☐ This application is a ☐ Continuation ☐ Division ☐ Continuation-in-part (CIP)
of application Serial No. Filed on
- ☐ This application claims priority of provisional application Serial No. Filed

17. CORRESPONDENCE ADDRESS

BLANK ROME COMISKY & MCCAULEY LLP
THE FARRAGUT BUILDING
SUITE 1000
900 17TH STREET, NW
WASHINGTON, DC 20006
TEL (202) 530-7400
FAX (202) 463-6915

Name:	Michael C. Greenbaum	Registration No.:	28,419
Signature:		Date:	March 31, 2000

Docket No. 000687.00138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S) José TAMEZ-PEÑA, Saara Marjatta Sofia TOTTERMAN and Kevin J. PARKER

SERIAL NO: New Application

FILING DATE: Herewith

FOR: MAGNETIC RESONANCE IMAGING WITH RESOLUTION AND CONTRAST ENHANCEMENT

FEE TRANSMITTAL

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

FOR	NUMBER FILED	NUMBER EXTRA	RATE	CALCULATIONS
TOTAL CLAIMS	53 - 20 =	33	× \$18 =	\$594.00
INDEPENDENT CLAIMS	4 - 3 =	1	× \$78 =	\$78.00
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIMS (If applicable)			+ \$260 =	\$0.00
<input type="checkbox"/> LATE FILING OF DECLARATION			+ \$130 =	\$0.00
BASIC FEE				\$690.00
TOTAL OF ABOVE CALCULATIONS				\$1,362.00
<input checked="" type="checkbox"/> REDUCTION BY 50% FOR FILING BY SMALL ENTITY				-\$681.00
<input type="checkbox"/> FILING IN NON-ENGLISH LANGUAGE			+ \$130 =	\$0.00
<input checked="" type="checkbox"/> RECORDATION OF ASSIGNMENT			+ \$40 =	\$40.00
TOTAL				\$721.00

- ☒ Please charge Deposit Account No. 23-2185 in the amount of **\$721.00**. A duplicate copy of this sheet is enclosed.
- ☐ A check in the amount of _____ to cover the filing fee is enclosed.
- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required for the papers being filed herewith and for which no check is enclosed herewith, or credit any overpayment to Deposit Account No. 23-2185. A duplicate copy of this sheet is enclosed.

Respectfully Submitted,

BLANK ROME COMISKY & MCCAULEY LLP

Date: 3/31/00

THE FARRAGUT BUILDING
SUITE 1000
900 17TH STREET, NW
WASHINGTON, DC 20008
TEL (202) 530-7400
FAX (202) 463-8915


Michael C. Greenbaum
Registration No. 28,419

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: José TAMEZ-PEÑA et al

GAU: none yet assigned

SERIAL NO: none yet assigned

EXAMINER: none yet assigned

FILED: concurrently herewith

FOR: MAGNETIC RESONANCE IMAGING WITH RESOLUTION AND CONTRAST ENHANCEMENT

SMALL ENTITY DECLARATION - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

Name of Nonprofit Organization: University of Rochester

Address of NonProfit Organization: 518 Hylan Building, Rochester, New York 14627-0140

Type of Nonprofit Organization:

- ☒ University or other institution of higher education
- ☐ Tax exempt under Internal Revenue Service Code (26 USC 501(a) and 501(c)(3))
- ☐ Nonprofit scientific or educational under statute of State of the United States of America
- Name of State: _____
- Citation of Statute: _____
- ☐ Would qualify as tax exempt under Internal Revenue Service Code (26 USC 501(a) and 501(c)(3)) if located in the United States of America
- ☐ Would qualify as nonprofit scientific or educational under statute of State of the United States of America if located in the United States of America
- Name of State: _____
- Citation of Statute: _____

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees to the United States Patent and Trademark Office regarding the invention described in

- ☒ the specification filed herewith.
- ☐ the application or patent described above.

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization regarding the above identified invention. If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights in the invention is listed below:

- ☒ no such person, concern or organization.
- ☐ Persons, concerns or organizations listed below. (NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities, 37 CFR 1.27)

Full Name	Address	Individual	Small Business Concern	Nonprofit Organization

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate; 37 CFR 1.28(b).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Name
Mark S. Coburn

Title
Acting Director

Signature

Date

Mark Coburn 3-29-00

APPLICATION FOR UNITED STATES LETTERS PATENT

TITLE: MAGNETIC RESONANCE IMAGING WITH RESOLUTION
AND CONTRAST ENHANCEMENT

INVENTORS: José TAMEZ-PEÑA
Saara Marjatta Sofia TOTTERMAN
Kevin J. PARKER

BLANK ROME COMISKY & McCAULEY LLP
Wigman, Cohen, Leitner & Myers IP Group
900 17th Street, N.W., Suite 1000
Washington, D.C. 20006
(202) 463-7700
(202) 463-6915 (facsimile)

Docket No. 000687.00138

MAGNETIC RESONANCE IMAGING WITH RESOLUTION AND CONTRAST ENHANCEMENT

Background of the Invention

Field of the Invention

5 The present invention is directed to a system and method for improving the resolution and tissue contrast in MRI.

Description of Related Art

10 The best current source of raw image data for observation of a complex soft tissue and bone structure is magnetic resonance imaging (MRI). MRI involves the transmission of RF signals of predetermined frequency (e.g., approximately 15 MHz in some machines, the frequency depending upon the magnitude of magnetic fields employed and the magnetogyric ratio of the atoms to be imaged). Typically, exciting pulses of RF energy of a specific frequency are transmitted via an RF coil structure into an object to be imaged. A short time later, radio-frequency NMR responses are received via the same or a similar RF coil structure. Imaging information is derived from such RF responses.

15 In MRI, a common imaging technique is the formation of images of selected planes, or slices, of the subject being imaged. Typically the subject is located in the static magnetic field with the physical region of the slice at the geometric center of the gradient field. Generally, each gradient will exhibit an increasing field strength on one side of the field center, and a decreasing
20 field strength on the other side, both variations progressing in the direction of the particular gradient. The field strength at the field center will thus correspond to a nominal Larmor frequency for the MRI system, usually equal to that of the static magnetic field. The specific component of a gradient which causes the desired slice to be excited is called the slice selection gradient. Multiple slices are taken by adjusting the slice selection gradient.

However, MRI often introduces the following technical challenges. Many of the anatomical structures to be visualized require high resolution and present low contrast, since, for example, many of the musculoskeletal structures to be imaged are small and intricate. MRI involves the use of local field coils to generate an electromagnetic field; such local field coils form a non-uniform illumination field. MRI images can also be noisy.

In particular, MRI has the following limitations in resolution and tissue contrast. Although current MRI machines can achieve relatively high intra-plane resolution, the inter-slice resolution is not so good as the intra-plane resolution; also, the inter-slice resolution is limited by the ability of the system to stimulate a single spatial slice or section. Although tissue contrast can be adjusted by selecting the right pulse sequence, analysis of a single pulse sequence is not enough to differentiate among adjacent similar tissues. In other words, the resolution is typically poor in the out-of-plane dimension, and the contrast is typically low between soft tissue structures.

Summary of the Invention

It will be readily apparent from the foregoing that a need exists in the art to overcome the above-noted limitations of conventional MRI.

Therefore, it is an object of the present invention to increase inter-slice resolution.

It is another object of the present invention to improve tissue contrast.

It is still another object of the present invention to improve inter-slice resolution and tissue contrast simultaneously.

It is yet another object to provide a simple technique for image registration.

To achieve the above and other objects, the present invention is directed to a system and method for creating high-resolution MRI volumes and also high-resolution, multi-spectral MRI volumes. At least one additional scan is obtained in an orthogonal direction. Then, through a data fusion technique, the information from an original scan and an orthogonal scan are combined, so as to produce a high-resolution, 3D volume. In addition, one may use a different pulse sequence in the original orientation or in an orthogonal orientation, and a data fusion technique can be applied to register the information and then visualize a high-resolution, multi-spectral volume.

Brief Description of the Drawings

A preferred embodiment will be set forth in detail with reference to the drawings, in which:

Fig. 1 shows a block diagram of an MRI system according to the preferred embodiment;

Figs. 2 and 3 show flow charts showing steps performed in registering and fusing two images;

Fig. 4 shows a blurring effect caused by the correlation of the two images;

Figs. 5A-5C show a typical signal, its gradient and a comparison of the autocorrelations of the signal and its gradient, respectively;

Figs. 6A and 6B show two voxels scanned in orthogonal directions;

Fig. 6C shows the problem of deriving high-resolution information from the voxels of Figs. 6A and 6B;

Figs. 7A-7I show comparisons between the individual scans and the fused image;

Figs. 8A-8I show a comparison among simple fusion without registration, simple fusion after registration and complete fusion;

Figs. 9A-9I show fusion of orthogonal images without correlation;

Figs. 10A and 10B show images taken with three and four local receiver coils, respectively;

Figs. 11A and 11B show a two-band spectral image of a knee; and

Figs. 11C and 11D show principal components of the image of Figs. 11A and 11B.

Detailed Description of the Preferred Embodiment

A preferred embodiment of the present invention will now be set forth in detail with reference to the drawings.

Fig. 1 shows a block diagram of an MRI system 100 on which the present invention can be implemented. The system 100 uses an RF coil 102 and a gradient coil 104 to apply the required RF and gradient fields to the subject S. A spectrometer 106, acting under the control of a computer 108, generates gradient signals which are amplified by an X amplifier 110, a Y amplifier 112 and a Z amplifier 114 and applied to the gradient coil 104 to produce the gradient fields. The spectrometer 106 also generates RF signals which are amplified by an RF amplifier 116 and applied to the RF coil 102 to produce the RF fields. The free induction decay radiation from the sample S is detected by the RF coil 102 or by one or more local receiving coils 118 and applied to the spectrometer 106, where it is converted into a signal which the computer 108 can analyze.

The computer 108 should be sufficiently powerful to run a mathematical analysis package such as AVS, a product of Advanced Visualization Systems of Waltham, Massachusetts, U.S.A. Examples are the Apple Power Macintosh and any IBM-compatible microcomputer capable of running Windows 95, 98 or NT. The significance of the local receiving coils 118, and particularly of the number used, will be explained in detail below. The other components of the system 100 will be familiar to those skilled in the art and will therefore not be described in detail here.

The various techniques to enhance the images will now be described in detail.

Inter-Slice Resolution

The inter-slice resolution problem is solved by using two volumetric data sets where scanning directions are orthogonal to each other, and fusing them in a single high-resolution

image. Fig. 2 shows an overview of the process. First, in step 202, a first scan of the subject is taken. In step 204, a second scan of the subject is taken in a direction orthogonal to that of the first scan. Third, in step 206, the images are registered. Finally, in step 208, the images are fused. Fig. 3 shows the steps involved in image registration. In step 302, gradients of the image data are formed. In step 304, the gradients are correlated. In step 306, the correlation is maximized through a hill-climbing technique.

Although the fusion of the two volumes seems to be trivial, two issues have to be taken into account: 1) the registration among volumes scanned at different time (step 206) and 2) the overlapping of sampling voxel volumes (step 208). Those issues are handled in ways which will now be described.

Image Registration (Step 206)

The goal of image registration is to create a high-resolution 3D image from the fusion of the two data sets. Therefore, the registration of both volumes has to be as accurate as the in-plane resolution. The preferred embodiment provides a very simple technique to register two very similar orthogonal MRI images. The registration is done by assuming a simple translation model and neglecting the rotation among the two volumes, thus providing a fair model for small and involuntary human motion between scans.

An unsupervised registration algorithm finds the point (x, y, z) where the correlation between the two data sets is maximum. The Schwartz inequality identifies that point as the point where they match. Given two functions $u(x, y, z)$ and $v(x, y, z)$, the correlation is given by:

$$r(x, y, z) = u(x, y, z) * v(x, y, z) = \iiint u(\alpha, \beta, \gamma) v(x + \alpha, y + \beta, z + \gamma) d\alpha d\beta d\gamma.$$

If $u(x, y, z)$ is just a displaced version of $v(x, y, z)$, or in other words, $u(x, y, z) = v(x + \Delta x, y + \Delta y, z + \Delta z)$, then the maximum is at $(-\Delta x, -\Delta y, -\Delta z)$, the displacement between the functions.

In MRI, every voxel in the magnetic resonance image observes the average magnetization of an ensemble of protons in a small volume. The voxel can therefore be modeled as the correlation of the continuous image by a small 3D window. Let $g_1(x, y, z)$ and $g_2(x, y, z)$ be the sampled volumes at two orthogonal directions, which are given by:

$$\begin{aligned} g_1(x, y, z) &= f(x, y, z) * w_1(x, y, z) * \Pi(x, y, z) \\ g_2(x, y, z) &= f(x + \Delta x, y + \Delta y, z + \Delta z) * w_2(x, y, z) * \Pi(x, y, z) \end{aligned}$$

where $w_1(x, y, z)$ and $w_2(x, y, z)$ are the 3D windows for the two orthogonal scanning directions, $(\Delta x, \Delta y, \Delta z)$ is a small displacement, and $\Pi(x, y, z)$ is the sampling function. Therefore, the correlation of the two sampled volumes is

$$\begin{aligned} r(x, y, z) &= g_1(x, y, z) * g_2(x, y, z) \\ &= f(x + \Delta x, y + \Delta y, z + \Delta z) * f(x, y, z) * w_1(x, y, z) * w_2(x, y, z) * \Pi(x, y, z). \end{aligned}$$

That is just a blurred version of the original correlation; the exact location of the maxima is shaped by the blurring function $h(x, y, z) = w_1(x, y, z) * w_2(x, y, z)$. That is, the correlation is distorted by the function $h(x, y, z)$. Fig. 4 shows an idealized window function for $w_1(x, y, z)$ and $w_2(x, y, z)$ and its corresponding supporting region of the blurring function, $h(x, y, z)$.

Finding the displacement using the above procedure works fine for noise-free data, but noise makes the search more difficult. Let $g_1(x, y, z) = (f(x, y, z) + n_1(x, y, z)) * w_1(x, y, z)$ and $g_2(x, y, z) = (f(x + \Delta x, y + \Delta y, z + \Delta z) + n_2(x, y, z)) * w_2(x, y, z)$ be the corresponding noisy volumes, where $n_1(x, y, z)$ and $n_2(x, y, z)$ are two uncorrelated noise sources. Thus, the correlation of g_1 and g_2 is given by

$$\begin{aligned} r(x, y, z) &= g_1(x, y, z) * g_2(x, y, z) \\ &= [f(x + \Delta x, y + \Delta y, z + \Delta z) * f(x, y, z) + \\ &\quad f(x + \Delta x, y + \Delta y, z + \Delta z) * n_1(x, y, z) + \\ &\quad f(x, y, z) * n_2(x, y, z)] * h(x, y, z) * \Pi(x, y, z), \end{aligned}$$

and the maximum is no longer guaranteed to be given by the displacement, especially for functions with smooth autocorrelation functions like standard MRI. The smooth autocorrelation functions make the error a function of the noise power. Autocorrelation functions whose shapes are closer to a Dirac delta function $\delta(x, y, z)$ are less sensitive to noise, which is the reason why many registration algorithms work with edges. The autocorrelation function of the gradient magnitude of standard MRI is closer to a Dirac delta function. Therefore, the registration of the gradient is less sensitive to noise.

Figs. 5A-5C shows a 1D example of the effect of the derivative on the autocorrelation function of a band-limited signal. Fig. 5A shows an original signal $f(x)$. Fig. 5B shows a smooth estimate of the magnitude of the derivative, namely,

$$g(x) = |f(x) * [-1 \quad -1 \quad 0 \quad 0 \quad 0 \quad 1 \quad 1]|$$

Fig. 5C shows autocorrelations; the dashed curve represents $f * f$, while the curve shown in crosses represents $g * g$. For that example, a smooth derivative operator is used to reduce the noise level.

For the above reasons, the automatic registration is based on finding the maximum on the correlation among the magnitude gradient of the two magnetic resonance images:

$$(\Delta x, \Delta y, \Delta z) = \text{Arg} \max_{(\Delta x, \Delta y, \Delta z)} \iiint \|\nabla g_1(\alpha, \beta, \gamma)\| \|\nabla g_2(\Delta x + \alpha, \Delta y + \beta, \Delta z + \gamma)\| d\alpha d\beta d\gamma.$$

In sampled images the gradient ∇ can be approximated by finite differences:

$$\|\nabla g(x, y, z)\| = \sqrt{d_x(x, y, z)^2 + d_y(x, y, z)^2 + d_z(x, y, z)^2},$$

where

$$d_x(x, y, z) = \frac{l(x, y, z) * g(x + \delta x, y, z) - l(x, y, z) * g(x - \delta x, y, z)}{2\delta x},$$

$$d_y(x, y, z) = \frac{l(x, y, z) * g(x, y + \delta y, z) - l(x, y, z) * g(x, y - \delta y, z)}{2\delta y},$$

$$d_z(x, y, z) = \frac{l(x, y, z) * g(x, y, z + \delta z) - l(x, y, z) * g(x, y, z - \delta z)}{2\delta z},$$

where δx , δy , δz are the sampling rates, and $l(x, y, z)$ is a low pass filter used to remove noise from the images and to compensate the differences between in-slice sampling and inter-slice sampling.

The maximization can be done using any standard maximization technique. The preferred embodiment uses a simple hill-climbing technique because of the small displacements. The hill-climbing technique evaluates the correlation at the six orthogonal directions: up, down, left, right, front and back. The direction that has the biggest value is chosen as the next position. That simple technique works well for the registration of two orthogonal data sets, as the one expects for involuntary motion during scans.

To avoid being trapped in local maxima and to speed up the process, a multi-resolution approach can be used. That multi-resolution approach selects the hill-climbing step as half the size of the previous step. Five different resolutions are used. The coarsest resolution selected is twice the in-plane resolution of the system, and the smallest size is just 25 percent of the in-plane resolution.

Even with a very simple optimization approach, the computation of the correlation of the

whole data set can be time consuming; therefore, the registration of two images can take time. To speed up the correlation of the two data sets, just a small subsample of the points with very high gradient are selected for use in the correlation process.

Some images suffer from a small rotation. In that case, the algorithm is extended to search for the image rotation. The same hill-climbing technique is used to find the rotation between images; but instead of doing the search in a three-dimensional space, the algorithm has to look at a six-dimensional space. That search space includes the three displacements and three rotations along each axis. At each step the rotation matrix is updated and used to compensate for the small rotation between images.

Image Fusion (Step 208)

Once the two images are registered, an isotropic high resolution image is created from them. Due to the different shape between voxel sampling volumes ($w_2(x, y, z)$ and $w_1(x, y, z)$), one has to be careful when estimating every high resolution voxel value from the input data. Assume that the first image has been scanned in the x -direction and the second has been scanned in the y -direction. Therefore, there is high-resolution information in the z -direction in both images.

Figs. 6A and 6B show the voxel shapes of the two input images, where the in-slice resolution is equal, and the inter-slice resolution is four times lower. Given that configuration, the problem of filling the high-resolution volume is a 2D problem. In a single 4×4 -voxel window of the high resolution image, as seen in Fig. 6C, then for every 16 high-resolution voxels there are only 8 known low-resolution voxels; therefore, that is an ill posed problem.

To address that problem, assume that every high-resolution voxel is just a linear combination of the two low-resolution functions:

$$g(x, y, z) = h_1(x / s_d, y, z) + h_2(x, y / s_d, z),$$

where h_1, h_2 are two functions which are back projected in such a way that

$$g_1(x/s_d, y, z) = \sum_{\forall x \in w_1} g(x, y, z),$$

$$g_2(x, y/s_d, z) = \sum_{\forall y \in w_2} g(x, y, z).$$

That represents a linear system with the same number of knowns as unknowns. The known values are the observed image voxels, while the values to back-project which match the observation are estimated. Noise and inhomogeneous sampling make the problem a little bit harder; but that linear system can efficiently be solved using projection on convex sets (POCS). Although, in theory, all the components have to be orthogonally projected, it can be shown that the following projecting scheme also works:

$$h_1^{k+1}(x/s_d, y, z) = h_1^k(x/s_d, y, z) - \alpha \frac{(nh_1^k(x/s_d, y, z) + \sum_{\forall x \in w_1} h_2^k(x, y/s_d, z) - g_1(x/s_d, y, z))n}{n^2 + m},$$

$$h_2^{k+1}(x, y/s_d, z) = h_2^k(x, y/s_d, z) - \alpha \frac{(mh_2^k(x, y/s_d, z) + \sum_{\forall y \in w_2} h_1^k(x/s_d, y, z) - g_2(x, y/s_d, z))m}{n + m^2},$$

where $0 < \alpha < 1$, n = the window size of w_1 , m = the window size of w_2 , $h_1^0(x, y, z) = g(x, y, z)$ and $h_2^0(x, y, z) = g_2(x, y, z)$ are the initial guesses for the estimation of back-projected functions.

The advantage of that approach over standard orthogonal projection is that is equations are simpler and that they can be implemented efficiently on a computer.

Experimental Data

Some experimental data produced by the above technique will now be described.

Figs. 7A, 7B and 7C respectively show the original MRI sagittal scan, the original MRI axial scan and the fused image of a human shoulder seen along an axial view. Figs. 7D, 7E and 7F show the same, except seen along a sagittal view. Figs. 7G, 7H and 7I show the same, except seen along a coronal view. In all three cases, the image is noticeably improved.

Figs. 8A, 8B and 8C show axial, sagittal and coronal slices, respectively, of simple fusion without registration. Figs. 8D, 8E and 8F show the same slices with simple fusion after registration. Figs. 8G, 8H and 8I show the same slices with complete image fusion. The simple fusion is $g(x, y, z) = 0.5 g_1(x, y, z) + 0.5 g_2(x, y, z)$, and the complete fusion is $g(x, y, z) = h_1(x, y, z) + h_2(x, y, z)$, wherein h_1 and h_2 are the two functions which minimize the reconstruction error.

Figs. 9A-9I show fusion of orthogonal images without correlation. Figs. 9A, 9B and 9C show axial views of the original MRI sagittal scan, the original axial scan and the fused image, respectively, for an axial view. Figs. 9D, 9E and 9F show the same for a sagittal view. Figs. 9G, 9H and 9I show the same for a coronal view.

Multiple Local Coil Receivers and Multispectral Imaging

Good signal-to-noise ratio is very important for an unsupervised segmentation algorithm. Even more important is the contrast-to-noise ratio among neighboring tissues. When local receiving coils are used, the signal from points far from the coil location is weak; therefore, contrast among tissues located far from the receiving coil is low. Some researchers have proposed several software alternatives to correct this signal fading, but this will increase the noise levels as well. Thus, it will not solve the problem. The preferred embodiment uses two or more receiving coils, which will improve the signal reception at far locations.

Figs. 10A and 10B show the advantage of using multiple coils. Fig. 10A shows an MRI

image of a knee using three surface coils. Fig. 10B shows an MRI image of the same knee using four surface coils.

Multispectral images will now be considered. Such images can be analogized to multispectral optical images, in which, for example, red, blue and green images are combined to create a single color image.

Figs. 11A and 11B show a two-band spectral image of a knee. Fig. 11A shows a cross section of a fat suppression MRI scan of the knee, where fat, and bone tissues have almost the same low density, cartilage has a very high density, and muscle tissue has a medium density. Fig. 11B shows the same knee, but now, muscle tissue and cartilage have the same density, making them very hard to differentiate. Those images clearly show the advantage of the multispectral image approach in describing the anatomy.

The analysis of a multispectral image is more complex than that of a single-spectrum image. One way to simplify the analysis is to reduce the number of bands by transforming an N -band multispectral image in such a way that passes the most relevant image into an $(N-n)$ -band image. The transform that minimizes the square error between the $(N-n)$ -band image and the N -band image is the discrete Karhuen-Loeve (K-L) transform. The resulting individual images from the transformed spectral image after applying the K-L transform are typically known as the principal components of the image.

Let the voxel \mathbf{x} be an N -dimensional vector whose elements are the voxel density from each individual pulse sequence. Then the vector mean value of the image is defined as

$$\mathbf{m}_x = E[\mathbf{x}] = \frac{1}{M} \sum_{k=1}^M \mathbf{x}_k,$$

and the covariance matrix is defined as

$$\mathbf{C}_x = E[(\mathbf{x} - \mathbf{m}_x)(\mathbf{x} - \mathbf{m}_x)^T] = \frac{1}{M} \sum_{k=1}^M \mathbf{x}_k \mathbf{x}_k^T - \mathbf{m}_x \mathbf{m}_x^T,$$

where M is the number of voxels in the image.

Because \mathbf{C}_x is real and symmetric, a set of n orthogonal eigenvectors can be found. Let \mathbf{e}_i and λ_i , $i = 1, 2, \dots, N$, be the eigenvectors and the corresponding eigenvalues of \mathbf{C}_x , so that $\lambda_j > \lambda_{j+1}$. Let \mathbf{A} be the matrix formed with the eigenvectors of \mathbf{C}_x . Then the transformation

$$\mathbf{y} = \mathbf{A}(\mathbf{x} - \mathbf{m})_x$$

is the discrete K-L transform, and y_i , $i = 1, 2, \dots, N$, are the components of a multispectral image. Figs. 11C and 11D show the principal components of the two-band spectral image shown in Figs. 11A and 11B. The advantage of the K-L decomposition of a multispectral image is that the image with the highest contrast is associated with the highest eigenvalue of the correlation matrix, and the image associated with the smallest eigenvalues usually is irrelevant.

The high-contrast, multispectral images thus formed can be utilized for diagnosis and for input to post-processing systems, such as three-dimensional rendering and visualization systems. If the multispectral data are from orthogonal planes or are acquired with some misregistration, the registration and orthogonal fusion steps described herein can be employed to enhance the resolution and contrast.

While a preferred embodiment of the present invention has been set forth above, those skilled in the art who have reviewed the present disclosure will readily appreciate that other embodiments can be realized within the scope of the present invention. For example, while the invention has been disclosed as used with the hardware of Fig. 1, other suitable MRI hardware can be used. For that matter, the invention can be adapted to imaging techniques other than MRI, such as tomography. Also, while the scans are disclosed as being in orthogonal directions, they can be taken in two different but non-orthogonal directions. Therefore, the present invention

should be construed as limited only by the appended claims.

001230-1250120

What is claimed is:

1. A method of forming an image of a subject, the method comprising:

(a) scanning the subject in a first direction to take image data of a first plurality of slices;

(b) scanning the subject in a second direction which is different from the first direction

to take image data of a second plurality of slices;

(c) registering the first plurality of slices with the second plurality of slices; and

(d) fusing the first plurality of slices with the second plurality of slices to form the image.

2. The method of claim 1, wherein the second direction is orthogonal to the first direction.

3. The method of claim 1, wherein steps (a) and (b) are performed with magnetic resonance imaging.

4. The method of claim 1, wherein step (c) comprises maximizing a correlation based on the image data of the first and second pluralities of slices.

5. The method of claim 4, wherein the correlation is a correlation of gradients of the image data of the first and second pluralities of slices.

6. The method of claim 5, wherein the correlation is maximized through a hill-climbing technique.

7. The method of claim 6, wherein the hill-climbing technique is a multiresolution hill-climbing technique.

8. The method of claim 7, wherein:

steps (a) and (b) are performed with a device having an in-plane resolution; and

the multiresolution hill-climbing technique is performed with a plurality of resolutions including:

(i) a maximum resolution which is twice the in-plane resolution; and

(ii) a minimum resolution which is one-quarter of the in-plane resolution.

9. The method of claim 6, wherein the hill-climbing technique is used to determine both a relative displacement and a relative rotation between the first and second pluralities of slices.

10. The method of claim 5, wherein the correlation is a correlation of a subsample of the image data of the first plurality of slices with a subsample of the image data of the second plurality of slices, the subsamples being taken in accordance with gradients of the image data.

11. The method of claim 1, wherein:

the image data of the first plurality of slices have a low resolution in the first direction and a high resolution in directions orthogonal to the first direction;

the image data of the second plurality of slices have the low resolution in the second direction and the high resolution in directions orthogonal to the second direction; and

step (d) comprises fusing the first plurality of slices with the second plurality of slices such that the image has the high resolution in all directions.

12. The method of claim 11, wherein step (d) comprises treating the image as a linear combination of functions having the low resolution and deriving the functions from the image data of the first and second pluralities of slices.

13. The method of claim 12, wherein the functions are derived through an iterative process using the image data of the first and second pluralities of slices as initial assumptions for the functions.

14. The method of claim 1, wherein steps (a) and (b) are performed using MRI with a plurality of receiving coils.

15. The method of claim 14, wherein steps (a) and (b) are performed using at least three receiving coils.

16. The method of claim 15, wherein steps (a) and (b) are performed using at least four receiving coils.

17. The method of claim 1, wherein:

steps (a) and (b) are performed through MRI; and

the image data of the first plurality of slices and the image data of the second plurality of slices comprise image data having a plurality of spectral bands.

18. The method of claim 17, wherein step (d) comprises selecting a subplurality of the plurality of spectral bands to form the image.

19. The method of claim 18, wherein the subplurality of the plurality of spectral bands is selected by ranking the plurality of spectral bands in order of image contrast and selecting the spectral bands whose image contrast is highest.

20. The method of claim 19, wherein the plurality of spectral bands is ranked in order of image contrast by:

deriving a covariance matrix from the plurality of spectral bands;

deriving a set of orthogonal eigenvectors and a corresponding set of eigenvalues from the covariance matrix; and

ranking the orthogonal eigenvectors in order of their corresponding eigenvalues.

21. A method of forming an image of a subject, the method comprising:

(a) performing an MRI scan on the subject to take image data having a plurality of spectral bands; and

(b) forming the image from the image data.

22. The method of claim 21, wherein step (b) comprises selecting a subplurality of the plurality of spectral bands to form the image.

23. The method of claim 22, wherein the subplurality of the plurality of spectral bands is selected by ranking the plurality of spectral bands in order of image contrast and selecting the spectral bands whose image contrast is highest.

24. The method of claim 23, wherein the plurality of spectral bands is ranked in order of image contrast by:

deriving a covariance matrix from the plurality of spectral bands;

deriving a set of orthogonal eigenvectors and a corresponding set of eigenvalues from the

covariance matrix; and

ranking the orthogonal eigenvectors in order of their corresponding eigenvalues.

25. The method of claim 21, wherein step (a) is performed with a plurality of receiving coils.

26. The method of claim 25, wherein step (a) is performed using at least three receiving coils.

27. The method of claim 26, wherein step (a) is performed using at least four receiving coils.

28. A system for forming an image of a subject, the system comprising:

scanning means for (i) scanning the subject in a first direction to take image data of a first plurality of slices and (ii) scanning the subject in a second direction which is different from the first direction to take image data of a second plurality of slices; and

computing means for (i) registering the first plurality of slices with the second plurality of slices and (ii) fusing the first plurality of slices with the second plurality of slices to form the image.

29. The system of claim 28, wherein the second direction is orthogonal to the first direction.

30. The system of claim 28, wherein the scanning means comprises an MRI scanner.

31. The system of claim 28, wherein the computing means registers the first and second pluralities of slices by maximizing a correlation based on the image data of the first and second

pluralities of slices.

32. The system of claim 31, wherein the correlation is a correlation of gradients of the image data of the first and second pluralities of slices.

33. The system of claim 32, wherein the correlation is maximized through a hill-climbing technique.

34. The system of claim 33, wherein the hill-climbing technique is a multiresolution hill-climbing technique.

35. The system of claim 34, wherein:

the scanning means has an in-plane resolution; and

the multiresolution hill-climbing technique is performed with a plurality of resolutions including:

(i) a maximum resolution which is twice the in-plane resolution; and

(ii) a minimum resolution which is one-quarter of the in-plane resolution.

36. The system of claim 35, wherein the hill-climbing technique is used to determine both a relative displacement and a relative rotation between the first and second pluralities of slices.

37. The system of claim 32, wherein the correlation is a correlation of a subsample of the image data of the first plurality of slices with a subsample of the image data of the second plurality of slices, the subsamples being taken in accordance with gradients of the image data.

38. The system of claim 28, wherein:

the image data of the first plurality of slices have a low resolution in the first direction and a high resolution in directions orthogonal to the first direction;

the image data of the second plurality of slices have the low resolution in the second direction and the high resolution in directions orthogonal to the second direction; and

the computing means fuses the first plurality of slices with the second plurality of slices

such that the image has the high resolution in all directions.

39. The system of claim 38, wherein the computing means treats the image as a linear combination of functions having the low resolution and deriving the functions from the image data of the first and second pluralities of slices.

5 40. The system of claim 39, wherein the functions are derived through an iterative process using the image data of the first and second pluralities of slices as initial assumptions for the functions.

41. The system of claim 28, wherein the scanning means comprises an MRI scanner with a plurality of receiving coils.

10 42. The system of claim 41, wherein the plurality of receiving coils comprises at least three receiving coils.

43. The system of claim 42, wherein the plurality of receiving coils comprises at least four receiving coils.

15 44. The system of claim 28, wherein:
the scanning means comprises an MRI scanner; and
the image data of the first plurality of slices and the image data of the second plurality of slices comprise image data having a plurality of spectral bands.

45. The system of claim 41, wherein the computing means selects a subplurality of the plurality of spectral bands to form the image.

20 46. The system of claim 45, wherein the subplurality of the plurality of spectral bands is selected by ranking the plurality of spectral bands in order of image contrast and selecting the spectral bands whose image contrast is highest.

47. The system of claim 46, wherein the plurality of spectral bands is ranked in order of image contrast by:

deriving a covariance matrix from the plurality of spectral bands;
deriving a set of orthogonal eigenvectors and a corresponding set of eigenvalues from the covariance matrix; and

ranking the orthogonal eigenvectors in order of their corresponding eigenvalues.

5

48. A system for forming an image of a subject, the system comprising:

scanning means for performing an MRI scan on the subject to take image data having a plurality of spectral bands; and

computing means for forming the image from the image data.

10

49. The system of claim 48, wherein the computing means selects a subplurality of the plurality of spectral bands to form the image.

50. The system of claim 49, wherein the subplurality of the plurality of spectral bands is selected by ranking the plurality of spectral bands in order of image contrast and selecting the spectral bands whose image contrast is highest.

15

51. The system of claim 50, wherein the plurality of spectral bands is ranked in order of image contrast by:

deriving a covariance matrix from the plurality of spectral bands;

deriving a set of orthogonal eigenvectors and a corresponding set of eigenvalues from the covariance matrix; and

ranking the orthogonal eigenvectors in order of their corresponding eigenvalues.

20

52. The system of claim 48, wherein the scanning means comprises a plurality of receiving coils.

53. The system of claim 52, wherein the plurality of receiving coils comprises at least three receiving coils.

25

54. The system of claim 53, wherein the plurality of receiving coils comprises at least four receiving coils.

Abstract of the Disclosure

MRI scans typically have higher resolution within a slice than between slices. To improve the resolution, two MRI scans are taken in different, preferably orthogonal, directions. The scans are registered by maximizing a correlation between their gradients and then fused to form a high-resolution image. Multiple receiving coils can be used. When the images are multispectral, the number of spectral bands is reduced by transformation of the spectral bands in order of image contrast and using the transformed spectral bands with the highest contrast.

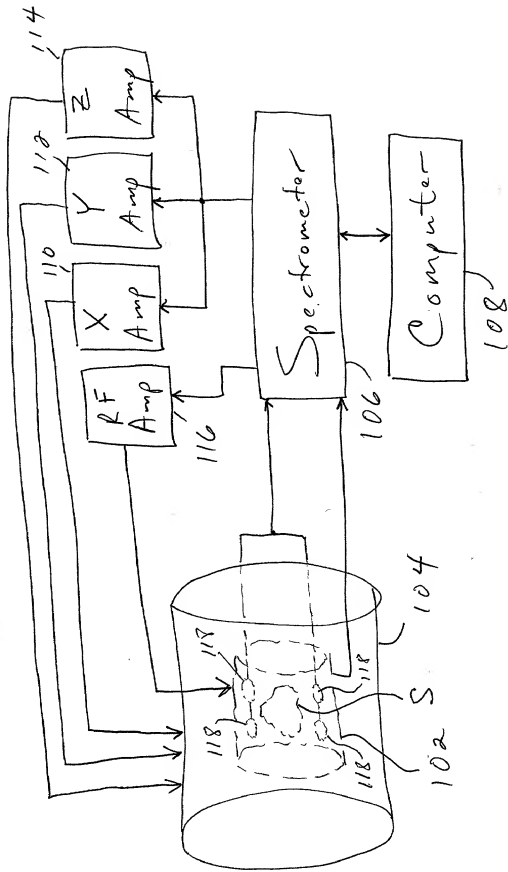


Fig. 1

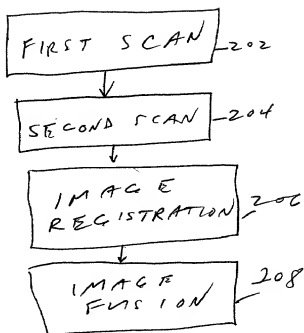


Fig. 2

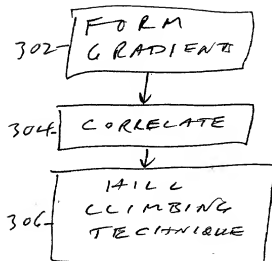


Fig. 3

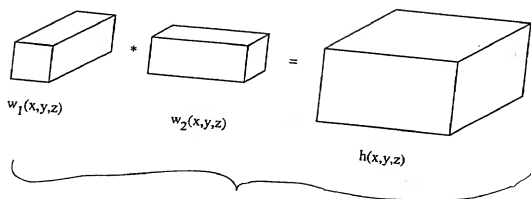


Fig. 4

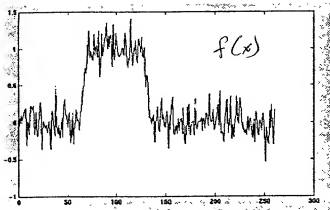


Fig. 5A

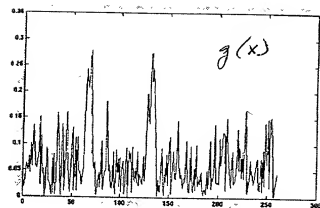


Fig. 5B

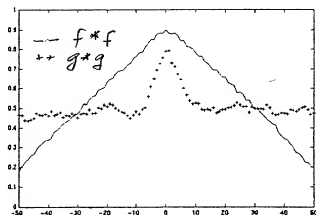


Fig. 5C

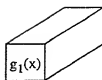


Fig. 6A

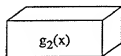


Fig. 6B

$g_2(y+3)$			$g(x+3, y+3)$
$g_2(y+2)$			
$g_2(y+1)$			
$g_2(y)$	$g(x, y)?$		
Known \nearrow	$g_1(x)$	$g_1(x+1)$	$g_1(x+2)$
		$g_1(x+3)$	

Fig. 6C



Fig. 7A

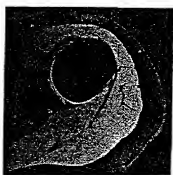


Fig. 7B



Fig. 7C



Fig. 7D



Fig. 7E



Fig. 7F



Fig. 7G



Fig. 7H



Fig. 7I

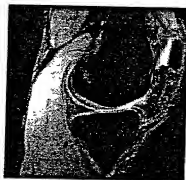


Fig. 8A



Fig. 8B



Fig. 8C



Fig. 8D



Fig. 8E



Fig. 8F



Fig. 8G



Fig. 8H

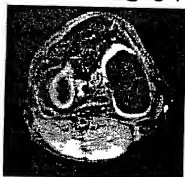


Fig. 8I



Fig. 9A



Fig. 9B



Fig. 9C



Fig. 9D



Fig. 9E



Fig. 9F



Fig. 9G



Fig. 9H



Fig. 9I



Fig. 10A



Fig. 10B



Fig. 11A

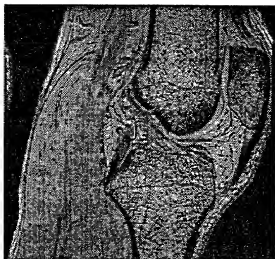


Fig. 11B

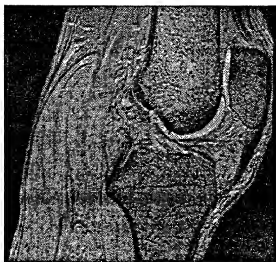


Fig. 11C



Fig. 11D

DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

MAGNETIC RESONANCE IMAGING WITH RESOLUTION AND CONTRAST ENHANCEMENT

the specification of which

☒ is attached hereto

☐ was filed on _____ as United States Application Number or PCT International Application Number _____ and (if applicable) was amended on _____

I hereby authorize our attorneys to insert the serial number assigned to this application.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 USC §119			
APPLICATION NO.	COUNTRY	DAY/MONTH/YEAR FILED	PRIORITY CLAIMED

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

PROVISIONAL APPLICATION(S) UNDER 35 U.S.C. §119(e)	
APPLICATION NUMBER	FILING DATE

I hereby claim the benefit under 35 U.S.C. §120 of any United States application, or §365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. §112.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

PRIOR U.S./PCT INTERNATIONAL APPLICATION(S) DESIGNATED FOR BENEFIT UNDER 37 U.S.C. §120		
APPLICATION NO.	FILING DATE	STATUS — PATENTED, PENDING, ABANDONED

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith: Herbert Cohen, Reg. No. 25,109; Victor M. Wigman, Reg. No. 25,201; George C. Myers, Jr., Reg. No. 27,040; Donald R. Greene, Reg. No. 22,470; Michael C. Greenbaum, Reg. No. 28,419; Charles R. Wolfe, Jr., Reg. No. 28,680; Michael D. White, Reg. No. 32,795; Karl O. Neidert, Reg. No. 39,313; David J. Edmondson, Reg. No. 35,126; Denise C. Lane, Reg. No. 42,780; Carl Schaukowitz, Reg. No. 29,211; James E. Howard, Reg. No. 39,715; Peter Weissman, Reg. No. 40,220 and Nicholas Bromer, Reg. No. 33,478.

BLANK ROME COMISKY & MCCAULEY, LLP

The Farragut Building
Suite 1000
900 17th Street, NW
Washington, DC 20006
TEL (202) 530-7400
FAX (202) 463-6915

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of sole or first inventor (given name, family name)

José TAMEZ-PEÑA

Signature

José Tamez-Peña

Date

3/30/2000

Residence

Rochester, New York

Citizenship

Mexico

Post Office

621 University Park, Rochester, New York 14620

Address

Full Name of additional joint inventor (given name, family name)

Saara Marjatta Sofia TOTTERMAN

Signature

Saara Totterman

Date

3/30/2000

Residence

Rochester, New York

Citizenship

Finland

Post Office

195 Dunrovin Lane, Rochester, New York 14618

Address

Full Name of additional joint inventor (given name, family name)

Kevin J. PARKER

Signature

Kevin J Parker

Date

3/30/2000

Residence

Rochester, New York

Citizenship

U.S.

Post Office

166 Superior Road, Rochester, New York 14625

Address

Full Name of additional joint inventor (given name, family name)

Signature

Date

Residence

Citizenship

Post Office

Address

Full Name of additional joint inventor (given name, family name)

Signature

Date

Residence

Citizenship

Post Office

Address

☐ Additional joint inventors are named on separately numbered sheets attached hereto.